**FUTURE TRENDS FOR CHRONIC KIDNEY DISEASE DIAGNOSIS, TREATMENT AND MANAGEMENT**

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**Abstract**

Chronic kidney disease (CKD) is the 16th leading cause of years of life lost worldwide. Appropriate screening, diagnosis, and management by primary care clinicians are necessary to prevent adverse CKD-associated outcomes, including cardiovascular disease, end-stage kidney disease, and death. CKD, which affects 8% to 16% of people globally, is described as a chronic impairment in kidney structure or function (such as a glomerular filtration rate [GFR] 60 mL/min/1.73 m2 or albuminuria 30 mg per 24 hours) for more than 3 months. The most typical causes of CKD in developed nations are diabetes and hypertension. Less than 5% of people with early CKD, however, claim to be aware of their condition. Staging and novel risk assessment techniques that take GFR and albuminuria into account can help direct therapy, monitoring, and referral strategies for those who have been diagnosed with CKD. Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers are effective in treating albuminuria, reducing the risk of cardiovascular disease, avoiding possible nephrotoxins like nonsteroidal anti-inflammatory medications, and treating CKD.

**Keywords:** Chronic Kidney diseases, Glomerular Filtrate Rate, Albuminuria, Angiotensin Converting Enzyme Inhibitors, Angiotensin II Receptors, , Hypertension, Anti-Inflammatory Medications.

1. **Introduction**

Between 8% and 16% of people worldwide are affected with chronic kidney disease (CKD), which is frequently overlooked by patients and medical professionals(1-4). Defined as having a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m2, albuminuria of at least 30 mg per 24 hours, or signs of kidney damage, such as persistent hematuria or anatomical abnormalities like polycystic or dysplastic kidneys, that last for longer than three months,(5) CKD is more prevalent in low- and middle-income than in high-income countries(6). The management and evaluation of CKD should use a risk-based approach, according to recent professional guidelines.(4)

1. **Methods**

It is a chronic renal failure; chronic renal insufficiency, epidemiology, incidence, prevalence, occurrence, diagnosis, assessment, identification, screening, workup, etiology, causes, management, treatment, intervention, therapy, and prevention were all searched for in a Medline and PubMed database up to April 2019. Results were limited to academic articles and guidelines written in English, studies involving humans, and human studies. 998 articles, including clinical trials, meta-analyses, practice recommendations, and systematic reviews, were found in the initial search. Later, the scope of the search was expanded to include review articles, observational studies, including cross-sectional studies, and more recent publications found in the reference lists of the articles that were found. Without regard to the size of the research or the patient population's age, all clinical studies for the treatment or prevention of CKD were included.

1. **Clinical presentations**

Typically, chronic kidney disease is discovered accidentally or through routine screening using urine and serum chemistry profiles. Patients may also experience symptoms including nocturia, flank pain, gross haematuria, "foamy urine" (an indication of albuminuria), nocturia, or decreased urine production.(7)

Patients with severe CKD may also have dyspnea, peripheral edema, fatigue, poor appetite, nausea, vomiting, metallic taste, unintentional weight loss, itching, and changes in mental status(7)

In evaluating a patient with known or suspected CKD, clinicians should inquire about additional symptoms that might suggest a systemic cause (eg, haemoptysis, rash, lymphadenopathy, hearing loss, neuropathy) or urinary obstruction (eg, urinary hesitancy, urgency, or frequency or incomplete bladder emptying. (7)

Furthermore, it is important to evaluate patients for factors that increase the risk of kidney disease. This includes considering whether they have previously been exposed to substances that could be harmful to the kidneys, such as nonsteroidalantiinflammatory drugs (NSAIDs), bowel preparations containing phosphate, herbal remedies containing aristolochic acid, antibiotic treatments like gentamicin, and chemotherapy. Other factors to consider are a history of kidneystones or recurring urinarytract infections, the presence of other health conditions like hypertension, diabetes, autoimmune disease, or chronic infections, a familyhistory of kidney disease, and any known genetic risk factors like sickle cell trait, if this information is available. (11,15)

A thorough physical examination should carefully assess the patient's volume status and may yield additional information about the underlying etiology of CKD. Signs of volume overload can result from decompensated heart failure, liver failure, or nephrotic syndrome, whereas signs of volume depletion might be caused by low oral intake, vomiting, diarrhoea, or over diuresis. On ocular examination, the presence of arterial-venous nicking or retinopathy suggests chronic hypertension or diabetes. Renovascular disease may be present in patients who have carotid or abdominal bruits. Consideration of obstructive uropathy, nephrolithiasis, pyelonephritis, or polycystic kidney disease should be made if there is flank pain or enlargement of the kidneys. Diabetes, vasculitis, or amyloidosis are less prevalent causes of neuropathy. Rash, palpable purpura, cryoglobulinemia, vasculitis, systemic lupus erythematosus, and acute interstitial nephritis are all possible skin symptoms. (7)

1. **CKD DEFINITION AND STAGING**

CKD is defined as the presence of abnormality both structure and function of kidney persisting more than 3 months. (5) One or more of the following are included in this: GFR less than 60 mL/min/1.73 m2, albuminuria (urine albumin less than 30 mg per 24 hours or urine albumin-to-creatinine ratio [ACR] less than 30 mg/g), abnormalities in urine sediment, histology, or imaging suggestive of kidney damage, renal tubular disorders, or transplantation history are all examples of kidney disease.  
(5)

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Once a diagnosis of CKD has been made, the next step is to determine staging, which is based on GFR, albuminuria, and cause of CKD ([Figure 2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/figure/F2/)).([5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/#R5)) Staging of GFR is classified as G1 (GFR ≥90 mL/min/1.73 m2), G2 (GFR 60–89 mL/min/1.73 m2), G3a (45–59 mL/min/1.73 m2), G3b (30–44 mL/min/1.73 m2), G4 (15–29 mL/min/1.73 m2), and G5 (<15 mL/min/1.73 m2) (5).

Furthermore, it is important to evaluate patients for any risk factors that may contribute to kidney disease, such as past exposure to substances that can be harmful to the kidneys (for example,(5,7,11)

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A urine ACR should preferably be used to measure albuminuria. There are three different levels of albuminuria staging: A1 (urine ACR 30 mg/g), A2 (30-300 mg/g), and A3 (>300 mg/g).According to 5 guidelines, urine ACR is preferred over urine protein-to-creatinine ratio for CKD staging because the latter's assays are more likely to be standardized and have superior precision at lower levels of albuminuria.(5) The most precise measurements come from a first morning sample or 24-hour collection, as there is high biological variability in urine albumin excretion over the course of the day.([5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/#R5),8,9) Random samples, however, are also acceptable in initial screening.[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/#R5) Compared with urine protein-to-creatinine ratio, urine ACR is believed to be a more sensitive and specific marker of glomerular pathology([5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/#R5))

Urine protein electrophoresis or testing for the particular protein (such as immunoglobulin heavy and light chains, 1-microglobulin, and 2-microglobulin) can be sought if tubular or overflow proteinuria is anticipated.5 In all patients with CKD, imaging with a kidney ultrasound to evaluate morphology and rule out urinary blockage should be taken into consideration.(5)

The location of anatomic abnormalities and the presence or absence of systemic disease are the two main factors used to classify the causes of CKD. Diabetes, autoimmune conditions, persistent infections, cancer, and hereditary disorders are a few examples of systemic diseases that impact other organs in addition to the kidney. Vascular, tubulointerstitial, glomerular, and cystic/congenital disorders are the categories used to categorize anatomic locations. (5)

1. **REDUCING RISK OF CARDIOVASCULAR DISEASES**

People with CKD have a much higher frequency of cardiovascular disease than people without CKD. For instance, in a Medicare 5% sample, 32% of the 1 086 232 people without CKD and 65% of the 175 840 adults aged 66 or older with CKD had cardiovascular disease.(10)Furthermore, having CKD is linked to poorer cardiovascular outcomes. For instance, in the same population, those with coronary artery disease (77% vs. 87%), acute myocardial infarction (69% vs. 82%), heart failure (65% vs. 76%), atrial fibrillation (70% vs. 83%), and cerebrovascular accident/transient ischemic attack (73% vs. 83%), all had lower 2-year survival rates when they had CKD.(10) Smoking cessation should also be encouraged.([5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/#R5))

1. **MANAGEMENT OF HYPERTENSION**

Many recommendations include algorithms that specify which medications should be used to treat hypertension in CKD patients (12,15) . Assessment of albuminuria's presence and severity is necessary. Adults with diabetes and a urine ACR of at least 30 mg per 24 hours or any adult with a urine ACR of at least 300 mg per 24 hours are advised to block the renin-angiotensin-aldosterone system with either an ACE-I or an angiotensin II receptor blocker (ARB) (5,11,12). Given the dangers of hyperkalaemia and acute renal injury, dual therapy with an ACE-I and an ARB is typically avoided (5,11,16).

1. **MANAGEMNT OF DIABETES MELLITUS**

It's crucial to control diabetes effectively. First, glycaemic management can halt the course of CKD; most recommendations call for a haemoglobin A1c target below 7.0%.Second, dosage modifications for oral hypoglycaemic medications can be required. Generally speaking, medications that are primarily eliminated by the kidneys (such as glyburide) should be avoided, whereas medications that are metabolized by the liver and/or partially eliminated by the kidneys (such as metformin and some DPP-4 and sodium-glucose cotransporter-2 [SGLT-2] inhibitors) may need to be dosed down or stopped altogether, especially when eGFR drops below 30 mL/min/1.73 m2.(11,14)

1. **NEPHROTOXINS**

The avoidance of nephrotoxins should be recommended to all individuals with CKD. A comprehensive list is outside the purview of this study, but a handful stand out. Routine NSAID administration in CKD is not advised, especially in patients on ACE-I or ARB therapy.(5,11)

1. **DRUG DOSING**

Most antibiotics, direct oral anticoagulants, gabapentin, pregabalin, oral hypoglycaemic medicines, insulin, chemotherapeutic agents, and opiates are examples of pharmaceuticals that frequently need dose decreases. (5,11)

Given the potential of developing nephrogenic systemic fibrosis, a painful and debilitating condition defined by significant fibrosis of the skin and occasionally other organs, gadolinium-based contrast agents are contraindicated in people with acute renal injury, eGFR less than 30 mL/min/1.73 m2, or ESKD. (5,11)

The best preventive may still be to stay away from gadolinium completely. Newer macrocyclic chelate formulations, such as gadoteridol, gadobutrol, or gadoterate, are far less likely to result in nephrogenic systemic fibrosis. In the event that gadolinium injection is deemed necessary, the patient must be informed about the possibility of developing nephrogenic systemic fibrosis, and a nephrologist may be consulted to discuss the possibility of post-exposure haemodialysis.(5,11)

1. **DIETARY MANAGEMENT**

Since big trials have had conflicting results, dietary treatment to stop CKD development is debatable. According to the MDRD study, which examined 2 levels of protein restriction in 840 patients, a low-protein diet resulted in a slower rate of GFR decline only after the first 4 months. However, a very low-protein diet compared to a low-protein diet was not significantly linked to a slower rate of GFR decline. The sub group with proteinuria more than 3 g per day appeared to benefit from both degrees of protein restriction, even though this group was tiny. (17). In adults with CKD stages G4–G5, the KDIGO guidelines advise limiting protein intake to less than 0.8 g/kg per day (with appropriate education) and to less than 1.3 g/kg per day in other adult patients with CKD at risk of progression.(5) The potential advantages of dietary protein limitation must be weighed against the risk of triggering protein wasting syndrome or malnutrition.(5,17),

1. **MONITORING OF ESTABLISHED CKD AND TREATMENT OF COMPLICATIONS**

The KDIGO guidelines advise monitoring albuminuria and eGFR at least once a year if CKD has been diagnosed. Patients at high risk should have these measures checked at least twice a year, and those at very high risk should have them checked at least three times a year (Figure 2). (5) Screening and frequency of assessment for laboratory abnormalities is dictated by stage of CKD and includes measurement of complete blood count, basic metabolic panel, serum albumin, phosphate, parathyroid hormone, 25-hydroxyvitamin D, and lipid panel ([Table](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/table/T1/)). ([5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/#R5)),

**Table.1 Screening, Monitoring, and Management of the Complications of Chronic Kidney Disease (CKD)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Complication** | **Relevant Tests** | **Frequency of Repeat Testing** | **Management** |
| Anaemia | Haemoglobin | No anaemia: CKD stages G1-G2: when clinically indicated CKD stage G3: at least once per year CKD stages G4-G5: at least twice per year With anaemia: CKD stages 3–5: at least every 3 months | Rule out other causes of anaemia: iron deficiency, vitamin B12 deficiency, folate deficiency, occult bleeding Consider iron supplementation and referral to a nephrologist for erythropoietin-stimulating agent therapy when haemoglobin <10 g/dL |
| Mineral and bone disorder | Serum calcium, phosphate, parathyroid hormone, 25-hydroxyvitamin D | Calcium/phosphate: CKD stage G3: every 6–12 months CKD stage G4: every 3–6 months CKD stage G5: every 1–3 months Parathyroid hormone: CKD stage G3: at baseline, then as needed CKD stage G4: every 6–12 months CKD stage G5: every 3–6 months Vitamin D: CKD stages 3–5: at baseline, then as needed | Consider phosphate-lowering therapy (eg, calcium acetate, sevelamer, iron-based binders) and vitamin D supplementation |
| Hyperkalemia | Serum potassium | At baseline and as needed | Low-potassium diet, correction of hyperglycaemia and acidemia, consider potassium binders |
| Metabolic acidosis | Serum bicarbonate | At baseline and as needed | Oral bicarbonate supplementation (eg, sodium bicarbonate, baking soda, or sodium citrate/citric acid) for values persistently <22 mmol/L |
| Cardiovascular disease | Lipid panel | At baseline and as needed | Low- to moderate-dose statin therapy for patients aged ≥50 years with CKD Statin therapy for patients aged 18–49 years with CKD and coronary artery disease, diabetes, prior ischemic stroke, or high risk of myocardial infarction or cardiovascular death |

Dietary restrictions and supplement prescriptions are frequently part of initial treatment plans. For patients with hyperkalaemia, primary care physicians should advise low-potassium diets, and for those with hyperphosphatemia, low-phosphorus diets.(5,11), Oral bicarbonate supplementation should be taken into consideration for individuals whose serum bicarbonate levels are chronically below 22 mmol/L because research suggests that long-term metabolic acidosis is linked to a higher rate of CKD progression. (5,11)

1. **REFERRAL TO A NEPHROLOGIST AND TRAING OF KIDNEY REPLACEMNT THERAPY**

According to the KDIGO guidelines, individuals with CKD should be sent to a nephrologist when their urine ACR rises above 300 mg per 24 hours (stage A3) or their eGFR drops below 30 mL/min/1.73 m2 (stage G4).(5) Albuminuria of more than 2200 mg per 24 hours should trigger an immediate nephrologist examination and the possibility of nephrotic syndrome. The following are other indications for referral: red blood cell casts on urine microscopy or other signs of glomerulonephritis, presence of more than 20 red blood cells per high-power field of unknown etiology, glomerulonephritis with uncontrolled hypertension despite the use of four or more antihypertensive medications, persistent hypokalaemia or hyperkalaemia, anaemia requiring erythropoietin replacement, recurrent or extensive kidney stones, hereditary kidney disease, acute kidney.

Primary care providers should try to find reversible causes because even slight changes in serum creatinine (e.g., from 0.7 mg/dL to 1.2 mg/dL) in people without CKD signal significant decreases in eGFR. The presence of cellular casts or abnormally shaped red blood cells in urine sediment, as well as an inexplicable or abrupt drop in GFR, are all indications for kidney biopsy, among other things.(5)

Otherwise, initiation of dialysis should be individualized and considered when patients have uremic signs or symptoms (eg, nausea, vomiting, poor appetite, metallic taste, pericardial rub or effusion, asterixis, or altered mental status), electrolyte abnormalities (eg, hyperkalaemia or metabolic acidosis), or volume overload (eg, pulmonary or lower extremity edema) refractory to medical management.([5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7015670/" \l "R5),11,)

**CONCLUSION:**

A primary cause of death, chronic kidney disease affects 8% to 16% of people globally. The best treatment for CKD is lowering cardiovascular risk, treating albuminuria, avoiding possible nephrotoxins, and adjusting medicine dosage. Additionally, patients need to be watched for CKD-related consequences include hyperkalaemia metabolic acidosis, anaemia, and other metabolic abnormalities. In order to lessen the burden of CKD globally, primary care doctors must correctly diagnose, stage, and refer patients with CKD.

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